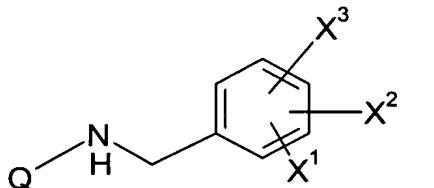


CLAIMS

1. A method of treating a disorder or condition selected from sleep disorders; autism; pervasive development disorder; rheumatoid arthritis; osteoarthritis; fibromyalgia; human immunodeficiency virus (HIV) infections; dissociative disorders such as body dysmorphic disorders; eating disorder such as anorexia and bulimia; ulcerative colitis; Crohn's disease; irritable bowel syndrome; functional abdominal pain; chronic fatigue syndrome; sudden infant death syndrome (SIDS); overactive bladder; chronic cystitis; chemotherapy induced cystitis; cough, angiotensin converting enzyme (ACE) induced cough; itch; hiccups; premenstrual syndrome; premenstrual dysphoric disorder; schizophrenia; schizoaffective disorder; delusional disorder; substance-induced psychotic disorder; brief psychotic disorder; shared psychotic disorder; psychotic disorder due to a general medical condition; schizophreniform disorder; amenorrheic disorders such as desmenorrhea; obesity; epilepsy; movement disorders such as primary movement disorders, spasticities, Scott's syndrome, Tourette's syndrome, palsys, amyolateral sclerosis (ALS), akinetic-rigid disorders, akinesias, dyskinesias, restless leg syndrome and movement disorders associated with Parkinson's disease or Huntington's disease; mastalgia syndromes; motion sickness; immune dysfunctions; generalized anxiety disorder; panic disorder; phobias, including social phobia, agoraphobia, and specific phobias; obsessive-compulsive disorder; post-traumatic stress disorder; depression including major depression, single episode depression, recurrent depression, child abuse induced depression, postpartum depression and dysthemia; cyclothymia; bipolar disorder; neurocardiac disorders such as neurocardiac syncope, neurogenic syncope, hypersensitive Carotid sinus, neurovascular syndrome and arrhythmias including arrythmias secondary to gastrointestinal disturbances; addiction disorders involving addictions to behaviors; HIV-1 associated dementia, AIDS dementia complex, HIV encephalopathy, HIV related neuralgias; AIDS related neuralgias; epilepsy; and attention deficit hyperactivity disorder in a mammal, comprising administering to said mammal an amount of a compound of the formula I,



wherein X¹ is hydrogen, (C₁-C₁₀) alkoxy optionally substituted with from one to three fluorine atoms or (C₁-C₁₀) alkyl optionally substituted with from one to three fluorine atoms;

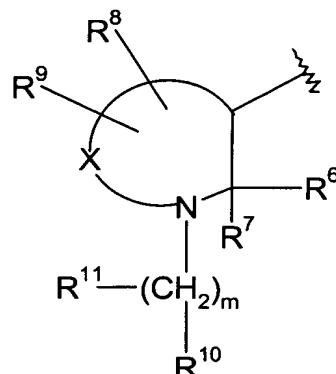
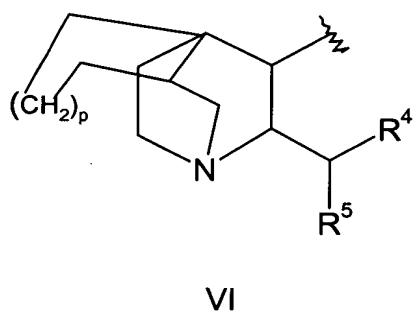
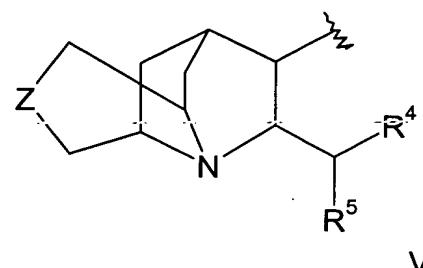
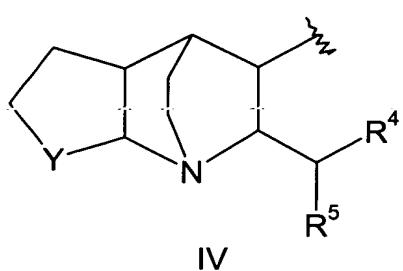
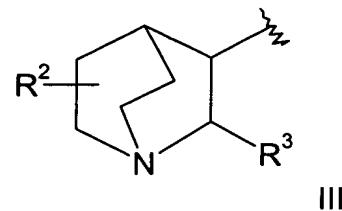
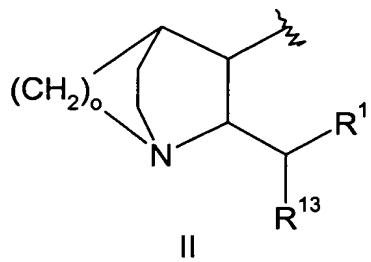
30 X² and X³ are independently selected from halo, hydrogen, nitro, (C₁-C₁₀) alkyl optionally substituted with from one to three fluorine atoms, (C₁-C₁₀) alkoxy optionally substituted with from one to three fluorine atoms, trifluoromethyl, hydroxy, phenyl, cyano, amino, (C₁-C₆)-alkylamino,

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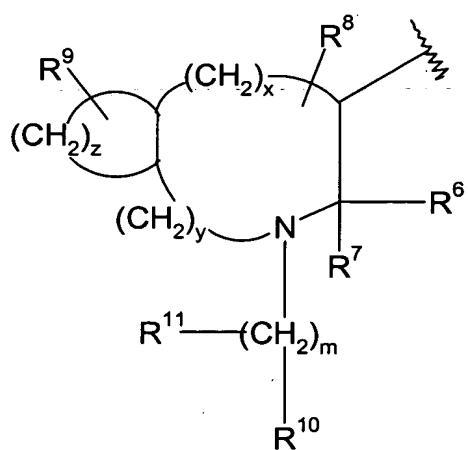
di-(C₁-C₆)alkylamino, -C(=O)-NH-(C₁-C₆)alkyl, (C₁-C₆)alkyl-C(=O)-NH-(C₁-C₆)alkyl, hydroxy(C₁-C₄)alkyl, (C₁-C₄)alkoxy(C₁-C₄)alkyl, -NHC(=O)H and -NHC(=O)-(C₁-C₆)alkyl; and

Q is a group of the formula

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OR



VIII

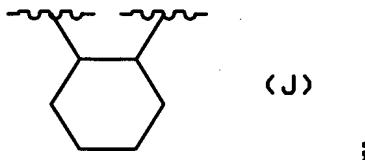
wherein R¹ is a radical selected from furyl, thienyl, pyridyl, indolyl, biphenyl and phenyl optionally substituted with one or two substituents independently selected from halo, (C₁-C₁₀) alkyl optionally substituted with from one to three fluorine atoms, (C₁-C₁₀) alkoxy optionally substituted with from one to three fluorine atoms, carboxy, benzyloxycarbonyl and (C₁-C₃) alkoxy-carbonyl;

5 R¹³ is selected from (C₃-C₄) branched alkyl, (C₅-C₆) branched alkenyl, (C₅-C₇) cycloalkyl, and the radicals named in the definition of R¹;

R² is hydrogen or (C₁-C₆) alkyl;

10 R³ is phenyl, biphenyl, naphthyl, pyridyl, benzhydryl, thienyl or furyl, and R³ may 10 optionally be substituted with from one to three substituents independently selected from halo, (C₁-C₁₀) alkyl optionally substituted with from one to three fluorine atoms and (C₁-C₁₀) alkoxy optionally substituted with from one to three fluorine atoms;

Y is (CH₂)_I wherein I is an integer from one to three, or Y is a group of the formula



15 Z is oxygen, sulfur, amino, (C₁-C₃)alkylamino or (CH₂)_n wherein n is zero, one or two; o is two or three;

p is zero or one;

x is an integer from zero to four;

y is an integer from zero to four;

20 z is an integer from one to six, and the ring in formula VIII containing (CH₂)_z may contain from zero to three double bonds, and one of the carbons of said (CH₂)_z may optionally be replaced by oxygen, sulphur or nitrogen;

25 R⁴ is furyl, thienyl, pyridyl, indolyl, biphenyl, or phenyl optionally substituted with one or two substituents independently selected from halo, (C₁-C₁₀) alkyl optionally substituted with from one to three fluorine atoms, (C₁-C₁₀) alkoxy optionally substituted with from one to three fluorine atoms, carboxy, (C₁-C₃) alkoxy-carbonyl and benzyloxycarbonyl;

R⁵ is thienyl, biphenyl or phenyl optionally substituted with one or two substituents independently selected from halo, (C₁-C₁₀) alkyl optionally substituted with from one to three fluorine atoms and (C₁-C₁₀) alkoxy optionally substituted with from one to three fluorine atoms;

30 X is (CH₂)_q wherein q is an integer from 1 to 6, and wherein any one of the carbon-carbon single bonds in said (CH₂)_q may optionally be replaced by a carbon-carbon double bond, and wherein any one of the carbon atoms of said (CH₂)_q may optionally be substituted with R⁸, and wherein any one of the carbon atoms of said (CH₂)_q may optionally be substituted with R⁹;

m is an integer from 0 to 8, and any one of the carbon-carbon single bonds of $(CH_2)_m$ may optionally be replaced by a carbon-carbon double bond or a carbon-carbon triple bond, and any one of the carbon atoms of said $(CH_2)_m$ having an available bonding site may optionally be substituted with R^{11} ;

5 R^6 is a radical selected from hydrogen, (C_1-C_6) straight or branched alkyl, (C_3-C_7) cycloalkyl wherein one of the carbon atoms may optionally be replaced by nitrogen, oxygen or sulfur; aryl selected from biphenyl, phenyl, indanyl and naphthyl; heteroaryl selected from thiienyl, furyl, pyridyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, triazolyl, tetrazolyl and quinolyl; phenyl (C_2-C_6) alkyl, benzhydrol and benzyl, wherein each of said aryl and heteroaryl groups and the
10 phenyl moieties of said benzyl, phenyl (C_2-C_6) alkyl and benzhydrol may optionally be substituted with one or more substituents independently selected from halo, nitro, (C_1-C_{10}) alkyl optionally substituted with from one to three fluorine atoms, (C_1-C_{10}) alkoxy optionally substituted with from one to three fluorine atoms, amino, hydroxy- (C_1-C_6) alkyl, (C_1-C_6) alkoxy- (C_1-C_6) alkyl, (C_1-C_6) -alkylamino, (C_1-C_6) alkyl-O-C(=O)-, (C_1-C_6) alkyl-O-C(=O)- (C_1-C_6) alkyl, (C_1-C_6) alkyl-C(=O)-O-,
15 (C_1-C_6) alkyl-C(=O)- (C_1-C_6) alkyl-O-, (C_1-C_6) alkyl-C(=O)-, (C_1-C_6) alkyl-C(=O)- (C_1-C_6) alkyl-, di- (C_1-C_6) alkylamino, -C(=O)NH- (C_1-C_6) alkyl, (C_1-C_6) alkyl-C(=O)-NH- (C_1-C_6) alkyl, -NHC(=O)H and -NHC(=O)- (C_1-C_6) alkyl; and wherein one of the phenyl moieties of said benzhydrol may optionally be replaced by naphthyl, thiienyl, furyl or pyridyl;

20 R^7 is hydrogen, phenyl or (C_1-C_6) alkyl;
or R^6 and R^7 , together with the carbon to which they are attached, form a saturated carbocyclic ring having from 3 to 7 carbon atoms wherein one of said carbon atoms may optionally be replaced by oxygen, nitrogen or sulfur;

25 R^8 and R^9 are each independently selected from hydrogen, hydroxy, halo, amino, oxo (=O), nitrile, hydroxy- (C_1-C_6) -alkyl, (C_1-C_6) alkoxy- (C_1-C_6) alkyl, (C_1-C_6) alkylamino, di- (C_1-C_6) alkylamino, (C_1-C_6) alkoxy, (C_1-C_6) alkyl-O-C(=O)-, (C_1-C_6) alkyl-O-C(=O)- (C_1-C_6) alkyl, (C_1-C_6) alkyl-C(=O)-O-, (C_1-C_6) alkyl-C(=O)- (C_1-C_6) alkyl-O-, (C_1-C_6) alkyl-C-, (C_1-C_6) alkyl-C(=O)- (C_1-C_6) alkyl-, and the radicals set forth in the definition of R^6 ;

30 R^{10} is $NHC(=O)R^{12}$, $NHCH_2R^{12}$, $NHSO_2R^{12}$ or one of the radicals set forth in any of the definitions of R^6 , R^8 and R^9 ;

35 R^{11} is oximino (=NOH) or one of the radicals set forth in any of the definitions of R^6 , R^8 and R^9 ; and

R^{12} is (C_1-C_6) alkyl, hydrogen, phenyl(C_1-C_6)alkyl or phenyl optionally substituted with (C_1-C_6) alkyl;

 with the proviso that (a) when m is 0, R^{11} is absent, (b) neither R^8 , R^9 , R^{10} nor R^{11} can form, together with the carbon to which it is attached, a ring with R^7 , (c) when Q is a group of the formula VIII, R^8 and R^9 cannot be attached to the same carbon atom, (d) when R^8 and R^9 are attached to the same carbon atom, then either each of R^8 and R^9 is independently selected from

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hydrogen, fluoro, (C₁-C₆) alkyl, hydroxy-(C₁-C₆)alkyl and (C₁-C₆)alkoxy-(C₁-C₆)alkyl, or R⁸ and R⁹, together with the carbon to which they are attached, form a (C₃-C₆) saturated carbocyclic ring that forms a spiro compound with the nitrogen-containing ring to which they are attached, (e) when neither X¹, X² nor X³ is a fluorinated alkoxy group, at least one of R¹, R³, R⁴, R⁵, R⁶, R⁷ and

5 R¹³ is an aryl group substituted with a fluorinated alkoxy group;
or a pharmaceutically acceptable salt thereof,
or a compound selected from the group consisting of:
(2S,3S)-3-(6-methoxy-3-trifluoromethyl-1,3-dihydroisobenzofuran-5-yl)methylamino-2-phenylpiperidine;

10 (2S,3S)-3-(6-methoxy-1-methyl-1-trifluoromethylisochroman-7-yl)methylamino-2-phenylpiperidine;
(2S,3S)-3-(6-methoxy-3-methyl-3-trifluoromethyl-1,3-dihydroisobenzofuran-5-yl)methylamino-2-phenylpiperidine;
(2S,3S)-3-(6-methoxy-3-phenyl-3-trifluoromethyl-1,3-dihydroisobenzofuran-5-yl)methylamino-2-phenylpiperidine;

15 (2S,3S)-3-[1-(6-methoxy-3-methyl-3-trifluoromethyl-1,3-dihydroisobenzofuran-5-yl)ethylamino]-2-phenylpiperidine;
(2S,3S)-3-[(1R)-6-methoxy-1-methyl-1-trifluoromethylisochroman-7-yl]methylamino-2-phenylpiperidine;

20 (2S,3S)-3-[(3R)-6-methoxy-3-methyl-3-trifluoromethyl-1,3-dihydroisobenzofuran-5-yl)methylamino-2-phenylpiperidine;
(2S,3S)-N-(5-ethyl-2-methoxyphenyl)methyl-2-diphenylmethyl-1-azabi-cyclo[2.2.2]-octan-3-amine;
(2S,3S)-N-(5-isopropyl-2-methoxyphenyl)methyl-2-di-phenylmethyl-1-azabicyclo[2.2.2]-

25 octan-3-amine;
(2S,3S)-N-(5-sec-butyl-2-methoxyphenyl)-methyl-2-diphenylmethyl-1-azabicyclo[2.2.2]-octan-3-amine;
(2S,3S)-N-(5-tert-butyl-2-methoxyphenyl)-methyl-2-diphenylmethyl-1-azabicyclo[2.2.2]-octan-3-amine; and

30 (2S,3S)-N-(5-methyl-2-methoxyphenyl)methyl-2-diphenylmethyl-1-azabicyclo[2.2.2]-octan-3-amine;
or a pharmaceutically acceptable salt thereof, that is effective in treating such disorder or condition.

2. A method according to claim 1, wherein the compound of formula I that is

35 employed in such method is selected from the following compounds and their pharmaceutically acceptable salts:

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2-(diphenylmethyl)-N-((2-difluoromethoxy)-phenyl)methyl-1-azabicyclo[2.2.2]octan-3-amine;

(2S,3S)-N-(2-methoxy-5-trifluoromethoxy-phenyl)methyl-2-diphenylmethyl-1-azabicyclo[2.2.2]octane-3-amine;

5 (2S,3S)-2-phenyl-3-[2-(2,2,2-trifluoroethoxy)-benzyl]aminopiperidine;

(2S,3S)-3-(2-methoxy-5-trifluoromethoxybenzyl)-amino-2-phenylpiperidine;

(2S,3S)-3-(2-hydroxy-5-trifluoromethoxybenzyl)-amino-2-phenylpiperidine;

(2S,3S)-2-phenyl-3-(3-trifluoromethoxybenzyl)-aminopiperidine;

(2S,3S)-1-(5,6-dimethoxyhexyl)-3-(2-methoxy-5-trifluoromethoxybenzyl)amino-2-

10 phenylpiperidine;

(2S,3S)-2-phenyl-3-(2-trifluoromethoxybenzyl)-aminopiperidine;

(2S,3S)-3-[5-chloro-2-(2,2,2-trifluoroethoxy)-benzyl]amino-2-phenylpiperidine;

(2S,3S)-3-(5-t-butyl-2-trifluoromethoxybenzyl)amino-2-phenylpiperidine;

15 3-(5-tert-butyl-2-methoxybenzyl)amino-2-(3-trifluoromethoxyphenyl)piperidine;

3-(2-isopropoxy-5-trifluoromethoxybenzyl)amino-2-phenyl)piperidine; and

3-(2-difluoromethoxy-5-trifluoromethoxybenzyl)-amino-2-phenylpiperidine.

3. A method according to claim 1, wherein the disorder or condition being treated is cyclothymia or bipolar disorder.

4. A method according to claim 1, wherein the disorder or condition being treated is an addiction to a behavior.

20 5. A method according to claim 1, wherein the disorder or condition being treated is a sleep disorder.

6. A method according to claim 1, wherein the disorder or condition being treated is premenstrual syndrome or premenstrual dysphoric disorder.

25 7. A method according to claim 1, wherein the disorder or condition being treated is autism or pervasive development disorder.

8. A method according to claim 1, wherein the disorder or condition being treated is Scott's syndrome or Tourette's syndrome.

9. A method according to claim 1, wherein the disorder or condition being treated is obsessive-compulsive disorder.

30 10. A method according to claim 1, wherein the disorder or condition being treated is selected from movement disorders such as primary movement disorders, spasticities, Scott's syndrome, Tourette's syndrome, palsys, amyolateral sclerosis (ALS), akinetic-rigid disorders, akinesias, dyskinesias, restless leg syndrome and movement disorders associated with Parkinson's disease or Huntington's disease.

11. A method according to claim 1, wherein the disorder or condition being treated is major depressive disorder.

12. A method according to claim 1, wherein the disorder or condition being treated is generalized anxiety disorder.

13. A method according to claim 1, wherein the disorder or condition being treated is irritable bowel syndrome.

5 14. A method according to claim 1, wherein the disorder or condition being treated is functional abdominal pain.

15. A method according to claim 1, wherein the disorder or condition being treated is an HIV infection.

10 16. A method according to claim 1, wherein the disorder or condition being treated is an immune dysfunction.

17. A method according to claim 1, wherein the disorder or condition being treated is selected from neurocardiac disorders such as neurocardiac syncope, neurogenic syncope, hypersensitive Carotid sinus, neurovascular syndrome and arrhythmias including arrhythmias secondary to gastrointestinal disturbances.

15 18. A method according to claim 1, wherein the disorder or condition being treated is selected from major depression, single episode depression, recurrent depression, child abuse induced depression, postpartum depression, dysthymia, cyclothymia and bipolar disorder.

20 19. A method according to claim 1, wherein the disorder or condition being treated is selected from as body dysmorphic disorders and eating disorders such as anorexia and bulimia.

25 20. A method according to claim 1, wherein the disorder or condition being treated is selected from schizophrenia, schizoaffective disorder, delusional disorder, substance-induced psychotic disorder, brief psychotic disorder, shared psychotic disorder, psychotic disorder due to a general medical condition, and schizopreniform disorder.

21. A method according to claim 1, wherein the disorder or condition being treated is selected from premenstrual syndrome, premenstrual dysphoric disorder, and amenorrheic disorders such as desmenorrhea.

30 22. A method according to claim 1, wherein the disorder or condition being treated is selected from Crohn's disease, ulcerative colitis, irritable bowel syndrome and functional abdominal pain.

23. A method according to claim 1, wherein the disorder or condition being treated is selected from autism, pervasive development disorder, and attention deficit hyperactivity disorder.

35 24. A method according to claim 1, wherein the disorder or condition being treated is selected from chronic fatigue syndrome, sudden infant death syndrome (SIDS), obesity, and epilepsy.

25. A method according to claim 1, wherein the disorder or condition being treated is selected from generalized anxiety disorder, panic disorder, obsessive-compulsive disorder, post-traumatic stress disorder, and phobias, including social phobia, agoraphobia, and specific phobias.

5 26. A method according to claim 1, wherein the disorder or condition being treated is selected from cough, angiotensin converting enzyme (ACE) induced cough, itch, and hiccups.

27. A method according to claim 1, wherein the disorder or condition being treated is selected from overactive bladder; chronic cystitis and chemotherapy induced cystitis.

10 28. A method according to claim 1, wherein the disorder or condition being treated is a sleep disorder.

29. A method according to claim 1, wherein the compound of formula I is administered to a human for the treatment of major depressive disorder and concomitant neuropathic pain.

15 30. A method according to claim 1, wherein the compound of formula I is administered to a human for the treatment of any two or more comorbid disorders or conditions selected from the disorders and conditions enumerated in claim 1.

31. A method according to claim 30, wherein the compound of formula I is administered to a human for the treatment of major depressive disorder and concomitant 20 generalized anxiety disorder.

35. A method according to claim 1, wherein the disorder or condition being treated is fibromyalgia.

36. A method according to claim 1, wherein the disorder or condition being treated is AIDS related neuralgia.

25 37. A method according to claim 1, wherein the disorder or condition being treated is schizophrenia, schizoaffective disorder, delusional disorder, substance-induced psychotic disorder, brief psychotic disorder, shared psychotic disorder, psychotic disorder due to a general medical condition, or schizopreniform disorder.

30 38. A method of treating a disorder or condition selected from the group consisting of sleep disorders; pervasive development disorder; rheumatoid arthritis; osteoarthritis; fibromyalgia; human immunodeficiency virus (HIV) infections; dissociative disorders such as body dysmorphic disorders; eating disorder such as anorexia and bulimia; ulcerative colitis; Crohn's disease; irritable bowel syndrome; functional abdominal pain; chronic fatigue syndrome; sudden infant death syndrome (SIDS); overactive bladder; chronic cystitis; chemotherapy 35 induced cystitis; cough, angiotensin converting enzyme (ACE) induced cough; itch; hiccups; premenstrual syndrome; premenstrual dysphoric disorder; schizophrenia; schizoaffective disorder; delusional disorder; substance-induced psychotic disorder; brief psychotic disorder;

shared psychotic disorder; psychotic disorder due to a general medical condition; schizophreniform disorder; amenorrheic disorders such as desmenorrhea; obesity; epilepsy; movement disorders such as primary movement disorders, spasticities, Scott's syndrome, Tourette's syndrome, palsys, amyolateral sclerosis (ALS), akinetic-rigid disorders, akinesias, 5 dyskinesias (e.g., familial paroxysmal dyskinesia, tardive dyskinesia, tremor, chorea, myoclonus, tics and other dyskinesias) restless leg syndrome and movement disorders associated with Parkinson's disease or Huntington's disease; mastalgia syndromes; motion sickness; immune dysfunctions; generalized anxiety disorder; panic disorder; phobias, including social phobia, agoraphobia, and specific phobias; obsessive-compulsive disorder; post-traumatic stress 10 disorder; depression including major depression, single episode depression, recurrent depression, child abuse induced depression, postpartum depression and dysthemia; cyclothymia; bipolar disorder; neurocardiac disorders such as neurocardiac syncope, neurogenic syncope, hypersensitive Carotid sinus, neurovascular syndrome and arrhythmias including arrhythmias secondary to gastrointestinal disturbances; addiction disorders involving 15 addictions to behaviors; HIV-1 associated dementia, AIDS dementia complex, HIV encephalopathy, HIV related neuralgias; AIDS related neuralgias; epilepsy; and attention deficit hyperactivity disorder in a mammal, including a human, comprising administering to said mammal an amount of a compound of the formula I, as defined in claim 1, that is effective in antagonizing the effect of substance P at its receptor site.

20 39. The present invention also relates to a method of treating a disorder or condition selected from the group consisting of pain resulting from soft tissue and peripheral damage, such as acute trauma; postherpetic neuralgia, trigeminal neuralgia, segmental or intercostal neuralgia and other neuralgias; pain associated with osteoarthritis and rheumatoid arthritis; musculo-skeletal pain, such as pain experienced after trauma; spinal pain, dental pain, 25 myofascial pain syndromes, episiotomy pain, and pain resulting from burns; deep and visceral pain, such as heart pain, muscle pain, eye pain, orofacial pain, for example, odontalgia, abdominal pain, gynaecological pain, for example, dysmenorrhoea, labour pain and pain associated with endometriosis; pain associated with nerve and root damage, such as pain associated with peripheral nerve disorders, for example, nerve entrapment and brachial 30 plexus avulsions, amputation, peripheral neuropathies, tic douloureux, atypical facial pain, nerve root damage, neuropathic lower back pain, HIV related neuropathic pain, diabetic neuropathic pain, and arachnoiditis; neuropathic and non-neuropathic pain associated with carcinoma, often referred to as cancer pain; central nervous system pain, such as pain due to spinal cord or brain stem damage; lower back pain; sciatica; phantom limb pain, headache, 35 including migraine and other vascular headaches, acute or chronic tension headache, cluster headache, temperomandibular pain and maxillary sinus pain; pain resulting from ankylosing spondylitis and gout; pain caused by increased bladder contractions; post operative pain; scar.

5 pain; and chronic non-neuropathic pain such as pain associated with fibromyalgia, HIV, rheumatoid and osteoarthritis, anthralgia and myalgia, sprains, strains and trauma such as broken bones; and post surgical pain in a mammal, including a human, comprising administering to said mammal an amount of a compound of the formula I, as defined in claim 1, or a pharmaceutically acceptable salt thereof, that is effective in treating such disorder or condition.

10 40. A method of treating a disorder or condition selected from the group consisting of pain resulting from soft tissue and peripheral damage, such as acute trauma; postherpetic neuralgia, trigeminal neuralgia, segmental or intercostal neuralgia and other neuralgias; pain associated with osteoarthritis and rheumatoid arthritis; musculo-skeletal pain, such as pain experienced after trauma; spinal pain, dental pain, myofascial pain syndromes, episiotomy pain, and pain resulting from burns; deep and visceral pain, such as heart pain, muscle pain, eye pain, orofacial pain, for example, odontalgia, abdominal pain, gynaecological pain, for example, dysmenorrhoea, labour pain and pain associated with endometriosis; pain associated with nerve and root damage, such as pain associated with peripheral nerve disorders, for example, nerve entrapment and brachial plexus avulsions, amputation, peripheral neuropathies, tic douloureux, atypical facial pain, nerve root damage, neuropathic lower back pain, HIV related neuropathic pain, diabetic neuropathic pain, and arachnoiditis; neuropathic and non-neuropathic pain associated with carcinoma, often referred to as cancer pain; central nervous system pain, such as pain due to spinal cord or brain stem damage; lower back pain; sciatica; phantom limb pain, headache, including migraine and other vascular headaches, acute or chronic tension headache, cluster headache, temperomandibular pain and maxillary sinus pain; pain resulting from ankylosing spondylitis and gout; pain caused by increased bladder contractions; post operative pain; scar pain; and chronic non-neuropathic pain such as pain associated with fibromyalgia, HIV, rheumatoid and osteoarthritis, anthralgia and myalgia, sprains, strains and trauma such as broken bones; and post surgical pain in a mammal, including a human, comprising administering to said mammal an amount of a compound of the formula I, as defined in claim 1, or a pharmaceutically acceptable salt thereof, that is effective in antagonizing the effect of substance P at its receptor site.

15 41. A method according to claim 38, wherein the disorder or condition that is being treated is neuropathic pain.

20 42. A method according to claim 38, wherein the disorder or condition that is being treated is AIDS related neuralgia.

25 43. A method according to claim 38, wherein the disorder or condition that is being treated is pain associated with fibromyalgia.

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44. A method according to claim 38, wherein the disorder or condition that is being treated is selected from neuropathic lower back pain, HIV related neuropathic pain, diabetic neuropathic pain, arachnoiditis and neuropathic and non-neuropathic pain associated with carcinoma.

5 45. A method according to claim 1, wherein the compound of the formula I that is employed in such method is:

(2S,3S)-3-(5-tert-butyl-2-methoxybenzyl)amino-2-(3-trifluoromethoxyphenyl)piperidine;

(2S,3S)-3-(2-isopropoxy-5-trifluoromethoxybenzyl)amino-2-phenyl-piperidine;

(2S,3S)-3-(2-ethoxy-5-trifluoromethoxybenzyl)amino-2-phenyl-piperidine;

10 (2S,3S)-3-(2-methoxy-5-trifluoromethoxybenzyl)-amino-2-phenylpiperidine;

(2S,3S)-3-(5-tert-butyl-2-trifluoromethoxybenzyl)amino-2-phenylpiperidine;

15 2-(diphenylmethyl)-N-(2-methoxy-5-trifluoromethoxy-phenyl)methyl-1-azabicyclo[2.2.2]octan-3-amine;

(2S,3S)-3-[5-chloro-2-(2,2,2-trifluoroethoxy)-benzyl]amino-2-phenylpiperidine;

20 (2S,3S)-3-(5-tert-butyl-2-trifluoromethoxybenzyl)amino-2-phenylpiperidine;

(2S,3S)-3-(2-isopropoxy-5-trifluoromethoxybenzyl)amino-2-phenylpiperidine;

(2S,3S)-3-(2-difluoromethoxy-5-trifluoromethoxybenzyl)-amino-2-phenylpiperidine;

(2S,3S)-2-phenyl-3-[2-(2,2,2-trifluoroethoxybenzyl)-aminopiperidine; or

(2S,3S)-2-phenyl-3-(2-trifluoromethoxybenzyl)]aminopiperidine;

25 or a pharmaceutically acceptable salt thereof.

46. A method according to claim 1, wherein the compound of formula I is administered to a human for the treatment of major depressive disorder and concomitant premenstrual dysphoric disorder.

47. A method according to claim 1, wherein the compound of formula I is administered to a human for the treatment of major depressive disorder and concomitant dysthymia.

48. A method according to claim 1, wherein the compound of formula I is administered to a human for the treatment of major depressive disorder and concomitant fibromyalgia.

30 49. A method according to claim 1, wherein the compound of formula I is administered to a human for the treatment of major depressive disorder and a concomitant somatoform disorder selected from somitization disorder, hypochondriasis, somatoform pain disorder and undifferentiated somatoform disorder.

50. A method according to claim 1, wherein the compound of formula I is administered to a human for the treatment of generalized anxiety disorder and concomitant irritable bowel syndrome.

51. A method according to claim 1, wherein the compound of formula I is administered to a human for the treatment of generalized anxiety disorder and concomitant functional abdominal pain.

52. A method according to claim 1, wherein the compound of formula I is administered to a human for the treatment of generalized anxiety disorder and concomitant neuropathic pain.

53. A method according to claim 1, wherein the compound of formula I is administered to a human for the treatment of generalized anxiety disorder and concomitant premenstrual dysphoric disorder.

10 54. A method according to claim 1, wherein the compound of formula I is administered to a human for the treatment of generalized anxiety disorder and concomitant dysthymia.

15 55. A method according to claim 1, wherein the compound of formula I is administered to a human for the treatment of generalized anxiety disorder and concomitant fibromyalgia.

56. A method according to claim 1, wherein the compound of formula I is administered to a human for the treatment of generalized anxiety disorder and a concomitant somatoform disorder selected from somitization disorder, hypochondriasis, conversion disorder, body dysmorphic disorder, somatoform pain disorder and undifferentiated somatoform disorder.

20 57. A method according to claim 1, wherein the compound of formula I is administered to a human for the treatment of major depressive disorder accompanied by one or more somatic symptoms selected from loss of appetite, sleep disturbances (e.g., insomnia, interrupted sleep, early morning awakening, tired awakening), loss of libido, restlessness, fatigue, constipation, dyspepsia, heart palpitations, aches and pains (e.g., headache, neck pain, back pain, limb pain, joint pain, abdominal pain), dizziness, nausea, heartburn, nervousness, tremors, burning and tingling sensations, morning stiffness, abdominal symptoms (e.g., abdominal pain, abdominal distention, gurgling, diarrhea), and the symptoms associated with generalized anxiety disorder.

30 58. A method according to claim 1, wherein the compound of formula I is administered to a human for the treatment of major depressive disorder accompanied by one or more somatic symptoms selected from fatigue, headache, neck pain, back pain, limb pain, joint pain, abdominal pain, abdominal distention, gurgling, diarrhea nervousness, and the symptoms associated with generalized anxiety disorder.

35 59. A method according to claim 1, wherein the compound of formula I is administered to a human for the treatment of generalized anxiety disorder accompanied by one or more somatic symptoms selected from loss of appetite, sleep disturbances (e.g., insomnia, interrupted sleep, early morning awakening, tired awakening), loss of libido,

PCT/US2015/048000

restlessness, fatigue, constipation, dyspepsia, heart palpitations, aches and pains (e.g., headache, neck pain, back pain, limb pain, joint pain, abdominal pain), dizziness, nausea, heartburn, nervousness, tremors, burning and tingling sensations, morning stiffness, abdominal symptoms (e.g., abdominal pain, abdominal distention, gurgling, diarrhea), and the 5 symptoms associated with major depressive disorder.

60. A method according to claim 1, wherein the compound of formula I is administered to a human for the treatment of generalized anxiety disorder accompanied by one or more somatic symptoms selected from fatigue, headache, neck pain, back pain, limb pain, joint pain, abdominal pain, abdominal distention, gurgling, diarrhea nervousness, and the 10 symptoms associated with major depressive disorder.

61. A method according to claim 11, wherein the mammal being treated is a human who has not exhibited an adequate treatment response following treatment for the same disorder or condition with a selective serotonin reuptake inhibitor.

62. A method according to claim 12, wherein the mammal being treated is a 15 human who has not exhibited an adequate treatment response following treatment for the same disorder or condition with a selective serotonin reuptake inhibitor.

63. A method according to claim 18, wherein the mammal being treated is a human who has not exhibited an adequate treatment response following treatment for the same disorder or condition with a selective serotonin reuptake inhibitor.

64. A method according to claim 21, wherein the mammal being treated is a 20 human who has not exhibited an adequate treatment response following treatment for the same disorder or condition with a selective serotonin reuptake inhibitor.

65. A method according to claim 25, wherein the mammal being treated is a human who has not exhibited an adequate treatment response following treatment for the same 25 disorder or condition with a selective serotonin reuptake inhibitor.

66. A method according to claim 1, wherein the disorder or condition being treated is selected from HIV-1 associated dementia, AIDS dementia complex, HIV encephalopathy, and HIV related neuralgias.

67. A method according to claim 1, wherein a Group A compound is employed in 30 such method.

68. A method according to claim 67, wherein the Group A compound that is employed in such method is selected from:

(2S,3S)-3-(6-methoxy-1-methyl-1-trifluoromethylisochroman-7-yl)methylamino-2-phenylpiperidine;

35 (2S,3S)-3-[(1R)-6-methoxy-1-methyl-1-trifluoromethylisochroman-7-yl]methylamino-2-phenylpiperidine;

(2S,3S)-N-(5-isopropyl-2-methoxyphenyl)methyl-2-di-phenylmethyl-1-azabicyclo[2.2.2]-octan-3-amine; and

(2S,3S)-N-(5-tert-butyl-2-methoxyphenyl)-methyl-2-diphenylmethyl-1-azabicyclo[2.2.2]-octan-3-amine;

5 and the pharmaceutically acceptable salts of such compounds.

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